

Appl. No. 09/623,138
Amdt. dated July 31, 2003
Reply to Office action of April 3, 2003

REMARKS

Claims 11, 14, 15, 17, 19 and 20 currently appear in this application. The Office Action of April 10, 2003, has been carefully studied. These claims define novel and unobvious subject matter under Sections 102 and 103 of 35 U.S.C., and therefore should be allowed. Applicants respectfully request favorable reconsideration, entry of the present amendment, and formal allowance of the claims.

Non-Finality of Office Action

Applicant's attorney wishes to thank Examiner Hui for the courtesies extended during the telephone interview of July 28, 2003. During that interview, Examiner Hui confirmed that the Office Action of April 3, 2003, was a non-final Action.

Rejections under 35 U.S.C. 112

Claims 11, 14-15, 17 and 19-20 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

This rejection is respectfully traversed. Claims 11, 17 and 19 have been amended to delete "prevention or" from the claims. Therefore, the claims

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presently under consideration are limited to treating the specific ocular inflammations recited therein.

Art Rejections

Claims 11, 14-15, 17 and 19-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Paul, Darn et al., and Muller et al. in view of Itoh et al. and Hingorani et al. Paul is said to teach that Langerhans cells is an antigen presenting cells that is highly effective in presenting antigen to T cells and that IL-1 increase the antigen presenting function of Langerhans cells to T cells. Niederkorn is said to teach that Langerhans cells are present in corneal epithelium and could migrate to the central cornea upon irritants or the presence of IL-1. Dam et al. are said to teach that calcitriol or calcipotriol inhibits TNF-alpha, a factor which can induce migration of Langerhans cells, which are a type of antigen presenting cells. Dam et al. are said to teach that calcitriol and calcipotriol are useful in suppressing the number of Langerhans cells when applied topically, and that calcitriol and calcipotriol suppress T-cell proliferation. Muller et al. are said to teach that calcitriol inhibits the production of IL-1 at a presecretory level such as by reducing the levels of interleukin-1 α mRNA, which is known to activate lymphocytes. The Examiner concedes that these references

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do not expressly teach that calcitriol is in a form of ophthalmic solution, nor that calcitriol is useful in treating keratoconjunctivitis, phlyctenular keratitis, or corneal infiltration. The Examiner further concedes that the references do not expressly teach that calcitriol is useful in a method to inhibit interleukin-1 production in corneal epithelium and thereby treat ocular inflammation.

Itoh et al. are said to teach that calcitriol can be formulated into an ophthalmic composition. Hingorani et al. are said to teach that atopic keratoconjunctivitis is a T-cell inflammation predominant disorder, and that atopic keratoconjunctivitis may lead to infiltration and corneal involvement such as epithelial keratitis.

This rejection is respectfully traversed. Claim 11 has been amended to recite that the compounds treat the ocular inflammations without lowering transparency of the cornea. Support of this limitation appears in the specification as filed at page 6, lines 17-19. As disclosed in the specification at page 9, lines 7-15, it is understood that a corneal transparency is lowered by a neovascularization in the cornea which occurs during the course of healing an ocular inflammation. According to the description in the specification appearing on page 12, lines 16-19 of the

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specification, IL-8 production is responsible for the neovascularization.

Figure 5 shows that calcitriol has an inhibitory effect on IL-8 production. In agreement with this, Figure 1 shows that calcitriol has an inhibitory effect on neovascularization. From these, it is clear that calcitriol has an ability to treat ocular inflammation without lowering corneal transparency.

None of the cited references discloses that a neovascularization in the cornea causes a lowered corneal transparency, that IL-8 is responsible for the neovascularization, and that calcitriol has an inhibitory effect on IL-8 production, thus preventing reduction of corneal transparency. Therefore, it is clear that one of ordinary skill in the art would not have been motivated by the cited references to administer the claimed compounds to treat the claimed ocular inflammations with the expectation that lowering of corneal transparency during the course of healing the ocular inflammations would be prevented.

In view of the above, it is respectfully submitted that the claims are now in condition for allowance, and favorable action thereon is earnestly

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solicited.

Respectfully submitted,

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